R E M A R K S

The Office Action of March 18, 2002, presents the examination of claims 20-39. Claims 20, 23, 27, 31, and 34 are amended. Claims 40 and 41 are added. Support for claims 40 and 41 is found in the specification, particularly on page 11, lines 7-16. No new matter is inserted into the application.

Specification (Page 2, paragraph 1 of the Office Action)

Applicants acknowledge with appreciation that the finality of the previous Office Action has been withdrawn. However, Applicants strongly disagree with the Examiner's assertion that Hong '765 (USP 6,165,765) receives priority to Application No. 08/544,643. As first presented in the Reply filed on March 4, 2002, it is clear that Hong '765 cannot receive priority to the '643 application.

Application No. 08/544,643 (USP 5,747,298) has a filing date of October 18, 1995. However, Hong '765 cannot receive priority back to this application because the DNA sequencing utilized in Hong '298 is totally different from the DNA sequence technique utilized in Hong '765. Specifically, Hong '298 only discloses and utilizes Sanger-type sequencing, wherein the nucleotide analogs utilized are terminating ddNTPs, i.e., ddNTPs

which, once incorporated into the nucleotide chain, terminate DNA amplification. It is known in the art that only one ddNTP can be placed into one tube and as such, the "two or more kinds of nucleotide analogs" element of the instant claims is not met. As such, the Examiner cannot rely on Hong's prior 08/544,643 application to antedate the instant filing date.

During the interview held with the Examiner on February 15, 2002, the Examiner agreed that Hong '765 could not receive priority from the prior applications Hong '298. Specifically, the Examiner wrote in the Interview Summary, "Applicants pointed out that Hong reference is not a prior art as this reference does not get priority of its CIP application. Therefore, 103(a) rejection is obviated."

However, as noted above, the Examiner appears to have changed his mind and writes in the outstanding Office Action that Hong '765 gets priority to application number 08/544,643. Nevertheless, the Examiner fails to explain his reasoning or provide any rationale whatsoever in making this decision. At the very least, the Examiner is requested to explain his assertion. However, the Examiner's acknowledgement that Hong '765 does not properly receive priority to either Application No. 08/544,643 (USP 5,747,298) or Application No. 08/642,684

(USP 5,834,253) is the most appropriate action and is therefore respectfully requested by Applicants.

Rejection under 35 U.S.C. § 102 (Page 2, paragraphs 2-3 of the Office Action)

The Examiner rejects claims 31-32 and 34-35 under 35 U.S.C. § 102(e) for allegedly being anticipated by Huse '762 (USP 5,681,726). Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

The Examiner asserts, "Huse '762 teaches at least one nucleotide analog to be incorporated in place of dGTP, dCTP, dATP, and dTTP and a reagent for synthesizing in the presence of nucleotide analog a cDNA that is complementary to an RNA."

However, Huse '726 discloses a method for the synthesis of double stranded DNA complementary to a selected RNA or DNA template, wherein a predetermined orientation of the double stranded DNA is preserved. In the method of Huse '726, a polynucleotide linker/primer comprising a restriction site and a nucleotide analog for protecting the double stranded DNA from cleavage by a corresponding restriction endonuclease are used,

in order to obtain double stranded DNA which has a directional invention complementary to a selected RNA or DNA template.

Huse '726 never teaches nor discloses that the term "methylated nucleotide analog" is equivalent to a combination of at least one nucleotide analog to be incorporated in place of dGTP or dCTP and at least one nucleotide analog to be incorporated in place of dATP or dTTP. Therefore, Huse '726 does not disclose each and every element of the instant claims.

In addition, Huse '726 neither teaches nor discloses that the use of the kit comprising both of the above-mentioned nucleotide analogs allows for the uniform incorporation of these nucleotide analogs into a targeted nucleic acid during amplification without influence of the GC content of the target RNA. The kit therefore allows for easy setting of the conditions for selective amplification of a product corresponding to RNA, which is not possible under the method of Huse '726.

Therefore, claims 31, 32, 34 and 35 are not anticipated by Huse '726. Withdrawal of the instant rejection is therefore respectfully requested.

Rejections under 35 U.S.C. § 103 (Pages 3-8, paragraphs 4-7 of the Office Action)

Huse '726 in view of Hong '298 (Paragraph 5 of the Office Action)

The Examiner rejects claims 20-25, 27-29, 31-32, 34-35, and 38-39 under 35 U.S.C. § 103(a) for allegedly being obvious over Huse '726 in view of Hong '298 (USP 5,747,298). Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

Huse '726 discloses a method for amplifying a DNA fragment containing a nucleotide analog via PCR. As acknowledged by the Examiner, Huse '726 fails to disclose a method for amplifying DNA in the presence of two or more kinds of nucleotide analogs. The Examiner attempts to make up for the deficiencies of Huse '726 by combining therewith the disclosure of Hong '298.

Hong '298 is directed to a novel DNA polymerase with proofreading ability useful for DNA sequencing. The DNA sequencing utilized in Hong '298 is Sanger-type sequencing, wherein the nucleotide analogs utilized are terminating ddNTPs, i.e., the ddNTPs terminate DNA amplification. The Examiner relies on column 3, lines 4-23 to support his assertion that the "two or more kinds of nucleotide analogs" element of the claims

is met. However, even if Hong '298 discusses more than one nucleotide analog, it still remains true that only one of those nucleotide analogs can be placed into one tube at a time.

In any event, to further distinguish the present invention from Hong '298, Applicants amend the claims to recite that the nucleotide analogs do not cause termination of the amplification. Support for this amendment is found on page 11, line 25 to page 12, line 6 of the specification. It is well known in the art that dideoxynucleotides (ddNTPs) cause termination of the amplification reaction. As such, the nucleotide analogs disclosed by Hong '298 are completely distinguishable from the instant nucleotide analogs.

Further, Applicants point out that Huse '726 neither teaches nor discloses the use of both of at least one nucleotide analog to be incorporated in place of dGTP or dCTP and at least one nucleotide analog to be incorporated in place of dATP or dTTP during the PCR amplification reaction. In addition, the use of both of the above-mentioned nucleotide analogs during amplification reaction allows for the uniform incorporation of these nucleotide analogs into targeted nucleic acid, without influence of the GC content of the target RNA.

In addition, although Hong '298 discloses in lines 10-20 of column 3 that during the sequencing reaction catalyzed by Bst DNA polymerase, all four dNTPs, including dCTP and other nucleotide analogs, such as dITP and 7-deaza-dGTP, are effectively incorporated equally into the nucleotide chain during elongation, Hong '298 neither teaches nor discloses the use of both of at least one nucleotide analog to be incorporated in place of dGTP or dCTP and at least one nucleotide analog to be incorporated in place of dATP or dTTP during the amplification reaction will achieve uniform incorporation of these nucleotide analogs into the targeted nucleic acid, without influence of the GC content of the target RNA.

Therefore, one of ordinary skill in the art would not be motivated to combine Huse '726 and Hong '298 for the purpose of specifically amplifying DNA of a target sequence derived from RNA. Even if these references were combinable, one of ordinary skill in the art would merely arrive at a method for sequencing comprising synthesizing a double stranded DNA by the use of Bst DNA polymerase, linker/primer, nucleotide analog for protecting the double stranded DNA, and dITP and/or 7-deaza-dGTP, thereby obtaining directional complementary DNA. For these reasons, the rejection is improper and should be withdrawn.

Rejection over Huse '726 in view of Hong '298 and further in view of Dodge '117 (Paragraph 6 of the Office Action)

The Examiner rejects claims 20-30, 31-32, 34-35, and 38-39 for allegedly being unpatentable over Huse '726 in view of Hong '298, and further in view of Dodge '117 (USP 5,912,117). Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

The Examiner relies on Dodge '117 to teach a compound for lowering Tm value. However, the hypothetical combination of these references still does not make the present invention obvious since none of the references disclose amplification in the presence of two or more nucleotide analogs, wherein the nucleotide analogs do not cause termination of the amplification.

For the above reasons, the rejection under 35 U.S.C. § 103 is improper and should be formally withdrawn on the record.

Rejection over Huse '726 in view of Hong '298 and further in view of Dodge '117 and the Stratagene Catalogue (Paragraph 7 of the Office Action)

The Examiner rejects claims 20-39 for allegedly being unpatentable over Huse '726 in view of Hong '298, and further in view of Dodge '117 and the Stratagene Catalogue. Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

The Examiner relies on the Strategene Catalogue to teach a kit. However, the hypothetical combination of these references still does not make the present invention obvious since none of the references disclose amplification in the presence of two or more nucleotide analogs, wherein the nucleotide analogs do not cause termination of the amplification.

For the above reasons, the rejection under 35 U.S.C. § 103 is improper and should be formally withdrawn on the record.

Conclusion

In summary, all of the present claims define patentable subject matter such that this application should be placed into condition for allowance. Early and favorable action on the merits of the present application is thereby requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Kristi L. Rupert, Ph.D. (Reg. No. 45,702) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Pursuant to the provisions of 37 C.F.R. § 1.17 and 1.136(a), Applicants hereby petition for an extension of two (2) months to August 18, 2002, for the period in which to file a response to the outstanding Office Action. The required fee of $400.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §1.16 or under 37 C.F.R. §1.17; particularly, extension of time fees.

Respectfully submitted,
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Attachment: Claim version with markings to show changes made